

AMENDMENTS TO THE CLAIMS

Please amend the claims as follows. This listing of claims will replace all prior versions, and listings, of claims in the applications:

Listing of Claims:

Claims 1-124. (canceled)

125. (currently amended) ~~The A polynucleotide comprising of claim 204, which comprises two nucleic acid subsequences and which encoded a TNF binding protein,~~

wherein the first nucleic acid subsequence encodes a soluble fragment of an insoluble human TNF receptor protein,

wherein said insoluble human TNF receptor protein (a) has an apparent molecular weight of about 75 kilodaltons as determined on a non-reducing SDS-polyacrylamide gel, (b) is encoded by a nucleic acid having the same sequence as a nucleic acid from a cDNA library made from HL-60 cell extracts, and (c) comprises the amino acid sequence LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10), and

wherein the second nucleic acid subsequence encodes all of the domains of the constant region of a human IgG immunoglobulin heavy chain other than the first domain of said constant region, and

wherein ~~said TNF binding recombinant protein exhibits specific TNF binding activity~~ the polynucleotide encodes a protein that specifically binds human TNF.

126. (canceled)

127. (previously presented) The polynucleotide of claim 125 wherein said soluble fragment comprises the amino acid sequence LCAP (SEQ ID NO:12).

128. (previously presented) The polynucleotide of claim 127 wherein said soluble fragment comprises the amino acid sequence VFCT(SEQ ID NO:8).

129. (previously presented) The polynucleotide of claim 128 wherein said soluble fragment comprises the amino acid sequence LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10).

130. (currently amended) The polynucleotide of claim ~~125, 128 or 129~~ 128 wherein said human immunoglobulin heavy chain is an IgG₁ heavy chain.

131. (canceled)

132. (currently amended) The polynucleotide of claim ~~129~~ 130 wherein the human immunoglobulin heavy chain ~~IgG~~ is an IgG₁ heavy chain.

Claims 133-147. (canceled)

148. (currently amended) The polynucleotide of claim ~~145~~ 129, wherein the second nucleic acid subsequence consists essentially of the immunoglobulin-encoding DNA sequence of pCD4H γ 1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5314) or of pCD4-H γ 3 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5523).

149. (currently amended) The polynucleotide of claim 148, wherein the second nucleic acid subsequence consists essentially of the immunoglobulin-encoding DNA sequences of pCD4-H γ 1 vector.

Claims 150-154 (canceled)

155. (currently amended) The polynucleotide of claim ~~125~~ 132, wherein the ~~TNF-binding-protein~~ that specifically binds human TNF consists of the soluble fragment and all the domains of the constant region of the human IgG immunoglobulin heavy chain other than the first domain of the constant region.

156. (currently amended) A vector comprising the polynucleotide of claim ~~125~~ 130.

157. (currently amended) A host cell comprising the polynucleotide of claim ~~425~~ 130.

158. (currently amended) A method of producing a protein that specifically binds human TNF, comprising the steps of:

- (a) culturing a host cell comprising the polynucleotide of claim ~~425~~ 130, and
- (b) isolating expressed protein that specifically binds human TNF from the cell mass or the culture medium.

159. (previously presented) The method of claim 158 wherein the host cell is a CHO cell.

Claims 160-212. (canceled)

213. (new) The method of claim 158, wherein the protein that specifically binds human TNF comprises the amino acid sequences LCAP (SEQ ID NO: 12) and VFCT (SEQ ID NO: 8).

214. (new) A polynucleotide comprising two nucleic acid subsequences, wherein the first subsequence encodes a human tumor necrosis factor (TNF)-binding soluble fragment of the human p75 TNF receptor amino acid sequence encoded by the cDNA insert of the plasmid deposited with the American Type Culture Collection (ATCC) on October 17, 2006 under Accession No. PTA 7942,

wherein the second subsequence encodes all of the domains of the constant region of a human immunoglobulin IgG heavy chain other than the first domain of said constant region, and

wherein the polynucleotide encodes a protein that specifically binds human TNF.

215. (new) The polynucleotide of claim 214, wherein the soluble fragment of the human p75 TNF receptor amino acid sequence comprises LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10).

216. (new) The polynucleotide of claim 215, wherein the IgG heavy chain is an IgG₁ heavy chain.

217. (new) The polynucleotide of claim 215, wherein the second subsequence consists essentially of the immunoglobulin-encoding DNA sequence of pCD4H γ 1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5314) or of pCD4-H γ 3 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5523).

218. (new) The polynucleotide of claim 217, wherein the second subsequence consists essentially of the immunoglobulin-encoding DNA sequence of pCD4H γ 1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5314).

219. (new) The polynucleotide of claim 216, wherein the protein that specifically binds human TNF consists of the soluble fragment and all of the domains of the constant region of the human immunoglobulin IgG heavy chain other than the first domain of said constant region.

220. (new) A vector comprising the polynucleotide of claim 215.

221. (new) A host cell comprising the polynucleotide of claim 215.

222. (new) A method of producing a protein that specifically binds human TNF, comprising the steps of:

(a) culturing the host cell of claim 221, and

(b) isolating expressed protein that specifically binds human TNF from the cell mass or the culture medium.

223. (new) The method of claim 222, wherein the host cell is a CHO cell.

224. (new) A polynucleotide comprising two nucleic acid subsequences, wherein the first subsequence encodes a human tumor necrosis factor (TNF)-binding soluble fragment of an insoluble human TNF receptor protein, wherein said insoluble human TNF receptor protein has the amino acid sequence of the insoluble receptor protein of SEQ ID NO:27,

wherein the second subsequence encodes all of the domains of the constant region of a human immunoglobulin IgG heavy chain other than the first domain of said constant region, and

wherein the polynucleotide encodes a protein that specifically binds human TNF.

225. (new) The polynucleotide of claim 224, wherein the IgG heavy chain is an IgG₁ heavy chain.

226. (new) The polynucleotide of claim 224, wherein the second subsequence consists essentially of the immunoglobulin-encoding DNA sequence of pCD4H γ 1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5314) or of pCD4-H γ 3 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5523).

227. (new) The polynucleotide of claim 226, wherein the second subsequence consists essentially of the immunoglobulin-encoding DNA sequence of pCD4H γ 1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5314).

228. (new) The polynucleotide of claim 225, wherein the protein that specifically binds human TNF consists of the soluble fragment and all of the domains of the

constant region of the human immunoglobulin IgG heavy chain other than the first domain of said constant region.

229. (new) A vector comprising the polynucleotide of claim 225.

230. (new) A host cell comprising the polynucleotide of claim 225.

231. (new) A method of producing a protein that specifically binds human TNF, comprising the steps of:

- (a) culturing the host cell claim 230, and
- (b) isolating expressed protein that specifically binds human TNF from the cell mass or the culture medium.

232. (new) The method of claim 231, wherein the host cell is a CHO cell.

233. (new) A polynucleotide comprising two nucleic acid subsequences, wherein the first subsequence encodes the extracellular region of an insoluble human tumor necrosis factor (TNF) receptor protein, wherein said insoluble human TNF receptor protein (a) has an apparent molecular weight of about 75 kilodaltons as determined on a non-reducing SDS-polyacrylamide gel, (b) is encoded by a nucleic acid having the same sequence as a nucleic acid from a cDNA library made from HL-60 cell extracts, and (c) comprises the amino acid sequences LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10),

wherein the second subsequence encodes all of the domains of the constant region of a human immunoglobulin IgG heavy chain other than the first domain of said constant region, and

wherein the polynucleotide encodes a protein that specifically binds human TNF.

234. (new) A polynucleotide of claim 233 wherein said insoluble human TNF receptor protein further comprises the amino acid sequences LCAP (SEQ ID NO: 12), VFCT (SEQ ID NO: 8), NQPQAPGVEASGAGEA (SEQ ID NO: 9) and VPHLPAD (SEQ ID NO: 13).

235. (new) The polynucleotide of claim 234, wherein the IgG heavy chain is an IgG₁ heavy chain.

236. (new) The polynucleotide of claim 233, wherein the second subsequence consists essentially of the immunoglobulin-encoding DNA sequence of pCD4H γ 1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5314) or of pCD4-H γ 3 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5523).

237. (new) The polynucleotide of claim 236, wherein the second subsequence consists essentially of the immunoglobulin-encoding DNA sequence of pCD4H γ 1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5314).

238. (new) The polynucleotide of claim 235, wherein the protein that specifically binds human TNF consists of the extracellular region and all of the domains of the constant region of the human immunoglobulin IgG heavy chain other than the first domain of said constant region.

239. (new) A vector comprising the polynucleotide of claim 235.

240. (new) A host cell comprising the polynucleotide of claim 235.

241. (new) A method of producing a protein that specifically binds human TNF, comprising the steps of:

- (a) culturing the host cell of claim 240 and
- (b) isolating expressed protein that specifically binds human TNF from the cell mass or the culture medium.

242. (new) The method of claim 241, wherein the host cell is a CHO cell.

243. (new) A polynucleotide comprising two nucleic acid subsequences,

wherein the first subsequence encodes the extracellular region of the human p75 TNF receptor amino acid sequence encoded by the cDNA insert of the plasmid deposited with the American Type Culture Collection (ATCC) on October 17, 2006 under Accession No. PTA 7942,

wherein the second subsequence encodes all of the domains of the constant region of a human immunoglobulin IgG heavy chain other than the first domain of said constant region, and

wherein the polynucleotide encodes a protein that specifically binds human TNF.

244. (new) The polynucleotide of claim 243, wherein the extracellular region of the p75 TNF receptor amino acid sequence comprises LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10).

245. (new) The polynucleotide of claim 243, wherein the protein that specifically binds TNF consists of the extracellular region and all of the domains of the constant region of a human immunoglobulin IgG₁ heavy chain other than the first domain of said constant region.

246. (new) The polynucleotide of claim 243, wherein the IgG heavy chain is an IgG₁ heavy chain.

247. (new) The polynucleotide of claim 246, wherein the second subsequence consists essentially of the immunoglobulin-encoding DNA sequence of pCD4Hγ1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5314) or of pCD4-Hγ3 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5523).

248. (new) The polynucleotide of claim 247, wherein the second subsequence consists essentially of the immunoglobulin-encoding DNA sequence of

pCD4Hy1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5314).

249. (new) A vector comprising the polynucleotide of claim 246.

250. (new) A host cell comprising the polynucleotide of claim 246.

251. (new) A method of producing a protein that specifically binds human TNF, comprising the steps of:

(a) culturing the host cell of claim 250 and

(b) isolating expressed protein that specifically binds human TNF from the cell mass or the culture medium.

252. (new) The method of claim 251, wherein the host cell is a CHO cell.

253. (new) A polynucleotide comprising two nucleic acid subsequences, wherein the first subsequence encodes the extracellular region of an insoluble human TNF receptor protein, wherein said insoluble human TNF receptor protein has the amino acid sequence of the insoluble receptor protein of SEQ ID NO:27,

wherein the second subsequence encodes all of the domains of the constant region of a human immunoglobulin IgG heavy chain other than the first domain of said constant region, and

wherein the polynucleotide encodes a protein that specifically binds human TNF.

254. (new) The polynucleotide of claim 253, wherein the protein that specifically binds TNF consists of the extracellular region and all of the domains of the constant region of a human immunoglobulin IgG₁ heavy chain other than the first domain of said constant region.

255. (new) The polynucleotide of claim 253, wherein the IgG heavy chain is an IgG₁ heavy chain.

256. (new) The polynucleotide of claim 253, wherein the second subsequence consists essentially of the immunoglobulin-encoding DNA sequence of pCD4H γ 1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5314) or of pCD4-H γ 3 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5523).

257. (new) The polynucleotide of claim 256, wherein the second subsequence consists essentially of the immunoglobulin-encoding DNA sequence of pCD4H γ 1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5314).

258. (new) A vector comprising the polynucleotide of claim 255.

259. (new) A host cell comprising the polynucleotide of claim 255.

260. (new) A method of producing a protein that specifically binds human TNF, comprising the steps of:

- (a) culturing the host cell of claim 259, and
- (b) isolating expressed protein that specifically binds human TNF from the cell mass or the culture medium.

261. (new) The method of claim 260, wherein the host cell is a CHO cell.

262. (new) A host cell comprising the polynucleotide of claim 155.

263. (new) A method of producing a protein that specifically binds human TNF, comprising the steps of:

- (a) culturing a host cell comprising the polynucleotide of claim 155, and
- (b) isolating expressed protein that specifically binds human TNF from the cell mass or the culture medium.

264. (new) A host cell comprising the polynucleotide of claim 219.

265. (new) A method of producing a protein that specifically binds human TNF, comprising the steps of:

- (a) culturing a host cell comprising the polynucleotide of claim 219, and
- (b) isolating expressed protein that specifically binds human TNF from the cell mass or the culture medium.

266. (new) A host cell comprising the polynucleotide of claim 228.

267. (new) A method of producing a protein that specifically binds human TNF, comprising the steps of:

- (a) culturing a host cell comprising the polynucleotide of claim 228, and
- (b) isolating expressed protein that specifically binds human TNF from the cell mass or the culture medium.

268. (new) A host cell comprising the polynucleotide of claim 238.

269. (new) A method of producing a protein that specifically binds human TNF, comprising the steps of:

- (a) culturing a host cell comprising the polynucleotide of claim 238, and
- (b) isolating expressed protein that specifically binds human TNF from the cell mass or the culture medium.

270. (new) A host cell comprising the polynucleotide of claim 245.

271. (new) A method of producing a protein that specifically binds human TNF, comprising the steps of:

- (a) culturing a host cell comprising the polynucleotide of claim 245, and
- (b) isolating expressed protein that specifically binds human TNF from the cell mass or the culture medium.

272. (new) A host cell comprising the polynucleotide of claim 254.

273. (new) A method of producing a protein that specifically binds human TNF, comprising the steps of:

- (a) culturing a host cell comprising the polynucleotide of claim 254, and
- (b) isolating expressed protein that specifically binds human TNF from the cell mass or the culture medium.